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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/802,220

03/17/2004

Masaki Sunami

227833

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23460

7590

10/28/2011

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CHICAGO, IL 60601-6731

EXAMINER

PAGONAKIS, ANNA

ART UNIT

PAPER NUMBER

1628

NOTIFICATION DATE

DELIVERY MODE

10/28/2011

ELECTRONIC

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

Chgpatent@leydig.com

<b>Office Action Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>	
	10/802,220	SUNAMI ET AL.	
	<b>Examiner</b>	<b>Art Unit</b>	
	ANNA PAGONAKIS	1628	

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 05 April 2011.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ An election was made by the applicant in response to a restriction requirement set forth during the interview on \_\_\_\_; the restriction requirement and election have been incorporated into this action.
- 4) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 5) ☒ Claim(s) 1-8 and 15-17 is/are pending in the application.
- 5a) Of the above claim(s) \_\_\_\_ is/are withdrawn from consideration.
- 6) ☐ Claim(s) \_\_\_\_ is/are allowed.
- 7) ☒ Claim(s) 1-8 and 15-17 is/are rejected.
- 8) ☐ Claim(s) \_\_\_\_ is/are objected to.
- 9) ☐ Claim(s) \_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 10) ☐ The specification is objected to by the Examiner.
- 11) ☐ The drawing(s) filed on \_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 12) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)            | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)   | Paper No(s)/Mail Date. ____.                                      |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>1 sheet; 7/12/2011</u> .                                      | 6) <input type="checkbox"/> Other: ____.                          |

### **DETAILED ACTION**

Applicant's amendment filed 4/5/2011 has been received and entered into the present application.

As reflected by the attached, completed copy form PTO/SB/08A (one page total), the Examiner has considered the cited references.

Applicant's arguments filed 4/5/2011 have been fully considered. Rejections not reiterated from previous Office Actions are hereby withdrawn. The following rejections are either reiterated or newly applied. They constitute the complete set of rejections presently being applied to the instant application.

The declaration under 37 C.F.R. 1.131 of Yoshifumi Uemoto has overcome the obviousness rejections previously set forth. As such the present obviousness rejection is newly presented.

### **Status of Claims**

Claims 1-8 and 15-17 are currently under examination and the subject matter of the present Office Action.

### ***Priority***

This application claims benefit of 60/455,293 filed 3/17/2003; 60/460,521 filed 4/4/2003; 60/477,202 filed 6/10/2003 and 60/493,649 filed 8/8/2003.

The later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original nonprovisional application or provisional application). The disclosure of the invention in the parent application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994).

The disclosure of the prior-filed applications, 60/455,293 filed 3/17/2003; 60/460,521 filed 4/4/2003; 60/477,202 filed 6/10/2003, fail to provide adequate support or enablement in the manner provided by the first paragraph of 35 U.S.C. 112 for one or more claims of this application. All claims

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are not adequately supported or enabled by the prior-filed applications the subject matter in claims 2-5 and 18. Specifically,

- (i) 60/455,293 fails to disclose the limitations of claims: 2-7 and 16-17;
- (ii) 60/460,521 fails to disclose the limitations of claims: 2-7 and 16-17;
- (iii) 60/477,202 fails to disclose the limitations of claims: 2-7 and 16-17;

It is noted that Applicant is not entitled to the priority date in these application for all claims in the instant claim set because the information contained within the previous referred filings does not support the granting of an earlier filing date. Applicant is invited to guide the Examiner to where the appropriate disclosure of the limitations for the above mentioned claims are found the respective priority documents.

*Response to Applicant Remarks*

*Applicant alleges that they do not believe that it is necessary to address the above remarks at this time.* As such, it remains that 60/455,293 filed 3/17/2003; 60/460,521 filed 4/4/2003; 60/477,202 filed 6/10/2003, fail to provide adequate support or enablement in the manner provided by the first paragraph of 35 U.S.C. 112 for one or more claims of this application.

***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 3-8 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The term “substantially” in claim 5, is a relative term which renders the claim indefinite. The term is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not reasonably be appraised of the scope of the

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invention. The term is unclear because meets and bound of "substantially" is not clear. For instance, is the cholesteryl ester transfer protein inhibitor 99.9 percent crystalline or 51 percent crystalline. For purposes of prosecution, the term "substantially" is interpreted as greater or equal to 50 percent crystalline

*Response to Applicant's Remarks*

*Applicant alleges that JTT-705 can only be crystalline or amorphous.* This is not commensurate in scope with the independent claim which is solely drawn to JTT-705 and does not require that it be in crystalline or amorphous form.

*Applicant alleges that "since claim 5 states that the amount of inhibitor in amorphous form does not exceed about 10 percent" this necessarily means that the inhibitor is 90 percent or more in crystalline form.* This is not found persuasive. Applicant's summarization of the breadth of the claim supports the rejection. Applicant states that the crystalline form is 90 percent *or more* (emphasis added). This is not possible since it would exceed the total of 100%. As such it remains that the term "substantially" is indefinite.

*Applicant alleges that it is clear that the specification describes how to ascertain the requisite degree of "substantially crystalline." Specifically, Applicant guides the Examiner to paragraph [0078].* This is not persuasive. It is not clear how the measurement of the possible crystalline content which x-ray diffraction, SEM analysis and DSC, provides a "requisite" degree of guidance with regard to the term "substantially". It appears that Applicant is implying that crystallization measurement techniques of paragraph [0078] can allow one to determine the amount of crystalline present. However, it remains that Applicant has not guided the Examiner as to where a definition of "substantially" is found in the specification.

**New rejection:**

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-8 and 15-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ault et al. (U.S. 2002/0123549) in view of Curatolo et al. (WO 2002/11710).

Ault et al. teaches a composition suitable for oral delivery of pharmaceutically active agents, comprising a therapeutically effective amount of a pharmacologically active agent; a crosspovidone or povidone; and a delivery agent for said pharmacologically active agents (abstract). Furthermore, the reference teaches the composition containing crosspovidone versus the comparative compositions which do not contain crosspovidone, resulting the greatly enhanced oral bioavailability of the formulations (paragraph [0084]).

Ault et al. is silent on the increasing the bioavailability of JTT-705.

Curatolo et al. teach that CETP inhibitors, such as the elected compound, S-[2-([-(2-ethylbutyl)cyclohexyl]carbonyl)amino)phenyl] 2-methyl propanethioate are generally hydrophobic and thus have extremely low solubility and thus have low oral bioavailability (claim 9, page 3). The CETP

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inhibitor is made in both amorphous and crystalline form, wherein the crystalline form does not exceed 10 percent and the amorphous form does not exceed 25 percent (page 9). The CEPT inhibitors are useful for the treatment of dyslipidemia, hyperbetalipoproteinemia, hypoalphalipoproteinemia, hypercholesterolemia, hypertriglyceridemia, cardiovascular disorders, angina, cardiac ischemia, myocardial infarction, hypertension and obesity (page 7).

One of ordinary skill in the art would have been motivated to substitute the pharmacologically active agent in Ault et al. with that of the claimed compound. One would have been motivated to do so and have a reasonable expectation of success because the claimed compound is known to have a low oral bioavailability while crosopovidone is known to achieve a great enhancement in oral bioavailability.

With respect to claim 7, the ratio of the CETP inhibitor, and crosopovidone is within the skill of the artisan at the time of the invention and would not have required undue experimentation or have been outside the realm of knowledge generally available to the skilled artisan. Factors that would have been taken into consideration when making such a determination would have included, but not have been limited to, the age, weight, sex, diet and medical condition of the patient, severity of the disease, route of administration, pharmacological considerations, e.g., activity, efficacy, pharmacokinetics and toxicology profiles of the particular compound employed, whether a drug delivery system is utilized and whether the compound is administered as part of a drug combination. Thus, the ratio that would have actually been employed would have been expected to vary widely and, in the absence of evidence to the contrary, would not have been inconsistent with that which is presently claimed.

### ***Double Patenting***

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the “right to exclude” granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir.

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1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-8 and 15-17 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-6, 10-11, 16-21, 34-40 and 53-58 of U.S. Patent 7,276,536 (Urata et al.) in view of Ault et al. (U.S. 2002/0123549) in view of Curatolo et al. (WO 2002/11710).

An obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but an examined application claim is not patentably distinct from the reference claims because the examined claims are either anticipated by, or would be obvious over the reference claims.

The claims of '536 are drawn increasing the bioavailability, increasing the absorption, treatment of a cardiovascular disorder and decreasing LDL with administration of the elected S-[2-([-(2-ethylbutyl)cyclohexyl]carbonyl)amino)phenyl] 2-methyl propanethioate.

The claims of '536 fail to teach (i) administration with crosopovidone; (ii) the crystalline form of to S-[2-([-(2-ethylbutyl)cyclohexyl]carbonyl)amino)phenyl] 2-methyl propanethioate as well as the AUC and activity of CETP in the bloodstream.

Ault et al. teaches a composition suitable for oral delivery of pharmaceutically active agents, comprising a therapeutically effective amount of a pharmacologically active agent; a crosopovidone or povidone; and a delivery agent for said pharmacologically active agents (abstract). Furthermore, the reference teaches the composition containing crosopovidone versus the comparative compositions which do not contain crosopovidone, resulting the greatly enhanced oral bioavailability of the formulations (paragraph [0084]).

Ault et al. is silent on the increasing the bioavailability of JTT-705.



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Curatolo et al. teach that CETP inhibitors, such as the elected compound, S-[2-([[(2-ethylbutyl)cyclohexyl]carbonyl]amino)phenyl] 2-methyl propanethioate are generally hydrophobic and thus have extremely low solubility and thus have low oral bioavailability (claim 9, page 3). The CETP inhibitor is made in both amorphous and crystalline form, wherein the crystalline form does not exceed 10 percent and the amorphous form does not exceed 25 percent (page 9). The CEPT inhibitors are useful for the treatment of dyslipidemia, hyperbetalipoproteinemia, hypoalphalipoproteinemia, hypercholesterolemia, hypertriglyceridemia, cardiovascular disorders, angina, cardiac ischemia, myocardial infarction, hypertension and obesity (page 7).

One of ordinary skill in the art would have been motivated to substitute the pharmacologically active agent in Ault et al. with that of the claimed compound. One would have been motivated to do so and have a reasonable expectation of success because the claimed compound is known to have a low oral bioavailability while crospovidone is known to achieve a great enhancement in oral bioavailability.

With respect to claim 7, the ratio of the CETP inhibitor, and crospovidone is within the skill of the artisan at the time of the invention and would not have required undue experimentation or have been outside the realm of knowledge generally available to the skilled artisan. Factors that would have been taken into consideration when making such a determination would have included, but not have been limited to, the age, weight, sex, diet and medical condition of the patient, severity of the disease, route of administration, pharmacological considerations, e.g., activity, efficacy, pharmacokinetics and toxicology profiles of the particular compound employed, whether a drug delivery system is utilized and whether the compound is administered as part of a drug combination. Thus, the ratio that would have actually been employed would have been expected to vary widely and, in the absence of evidence to the contrary, would not have been inconsistent with that which is presently claimed.

### CONCLUSION

No claim is found to be allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ANNA PAGONAKIS whose telephone number is (571)270-3505. The examiner can normally be reached on Monday thru Thursday, 7am to 5pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brandon Fetterolf can be reached on 571-272-2919. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

AP  
/Brandon J Fetterolf/  
Supervisory Patent Examiner, Art Unit 1628